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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/977,797 | 10/15/2001 | Jeffry D. Watkins | AME-06805 | 3451 |

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Eli Lilly and Company
Patent Division
P.O. Box 6288
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EXAMINER

WESSENDORF, TERESA D

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1639

DATE MAILED: 05/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/977,797

Applicant(s)

WATKINS ET AL.

Examiner

T. D. Wessendorf

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 February 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 6-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 6-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/10/2006 has been entered.

Status of Claims

Claims 1 and 6-25 are pending and under examination.

Claims 2-5 have been cancelled

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35

U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 25, as amended and added, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

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matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The negative limitation in claim 25 of "said phage expressed library is not expressed on the surface of a phage" is not supported in the as-filed specification. Applicants rely on page 18, lines 1-10 for support. A review of page 18 does not disclose said negative limitation. Rather, a phage and yeast methods. These specific methods would not support the broad above claimed negative limitation. The as-filed specification does not describe in specific terms the method that is not covered by the negative limitation i.e., the other surface by which a library is expressed.

Claim 1 drawn to a "...solid support comprises a membrane" is not supported in the as-filed specification. Applicants point out at page 4 of the REMARKES of 2/10/2006 that support for the new limitations can be found in the original claim 3 and page 27 to page 28, lines 1-9. A review of the sections relied upon do not recite for the newly added limitation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 6-25, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 7 is unclear as to the step of "treating a cell with said immunoglobulin". This is inconsistent with the base claim 1 which recites an anti-immunoglobulin (Ig) reagent.

2. There is a lack of antecedent basis for the phrase "surface expressed **cancer polypeptides**" in claim 15. The base claim does not recite said phrase.

5. The term "more" in claims 1 and 23 is a relative term which renders the claim indefinite. The term "more" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is suggested that the term "at least one" be used.

6. The term "less" in claim 24 is a relative term which renders the claim indefinite. The term "less" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in

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the art would not be reasonably apprised of the scope of the invention.

7. In claim 25 the phraseology "wherein said phage expressed library is not expressed on the surface of a phage" is inconsistent with the base claim from which it depends. The base claim 1 recited a phage expressed antibody library i.e., that the expressed antibody library is expressed on the phage. This claims broaden the base claim which does not recite any other surface expressing library but phage.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 7, 9, 13, 14, 20, 23 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Skerra et al (Analytical Biochemistry).

Skerra teaches a method of screening large numbers of bacterial colonies expressing Fab antibody fragments by

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selective capture of the secreted Fab fragments onto a membrane coated with anti-globulin antibody followed by addition of antigen and detection of binding by the immobilized antibody fragments. Thus, Skerra fully meet the instant limitations of identifying binding molecule from antibody expression libraries by selectively immobilizing the antibody followed by detection of binding to antigen. See the abstract; pages 153, first paragraph and pages 154, next to last paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6-16, 18-19 and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skerra view of Marks et al.

Skerra discussed supra, teaches screening assays for the determination of binding molecules wherein the binding molecules are selectively immobilized and bound to labeled antigen. Skerra

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fails to teach that the antigen is a tumor antigen. Marks teaches the desirability of production of and screening for human antibodies, via phage expression libraries, which antibodies are specific for tumor antigens. Further, the specific example provided is of a cell surface tumor antigen. Marks teaches the advantages of less non-specific killing by targeted immunotoxins and lowered immune reactivity to the immunotoxin. See col.1, lines 40-67; col.3, lines 24-40 and col. 13, lines 39-45. It would have been prima facie obvious to one having ordinary skill in the art to have been motivated to utilize the library screening methods of Skerra to screen antibody libraries for antibodies specific for tumor antigens, including cell surface tumor antigens with a reasonable expectation of success given the demonstration of Marks and the desirability to do so as taught by Marks.

Claims 17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skerra in view of Marks as applied to claims 1, 6-16, 18-9 and 21-25 above, and further in view of Yelton et al (EP 699,756) and Huse.

Skerra is discussed supra. Skerra does not teach that the antibody comprises goat anti-human kappa antibody and a nitrocellulose membrane. Yelton discloses at page 19, line 11 up to page 20, line 7, a method of contacting nitrocellulose

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filters blocked with a blocking buffer (page 26, lines 22-26) to prevent nonspecific binding of antibodies and coated with goat anti-human kappa light chain conjugated to alkaline phosphatase. And then contacted with phage BR antibody library. See further the cited Huse reference, (J.Immunol.) which describes the coating of support. See also, page 16, lines 5-50; page 24, lines 35-40. Yelton discloses at page 21, line 54 that the method further comprises binding the above BR96 with tumor cell line, H3396. See all the examples, specifically Example 5 at page 32. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use goat anti-human kappa antibody in the method of Skerra as taught by Yelton and Huse. One having ordinary skill in the art at the time the invention was made would be motivated to use a conventionally known Ig. One would reasonably expect to successfully use a method with a component that has been known in the art.

Claims 1, 6, 18-19 and 25, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowman et al (USP 6,172,213).

Lowman et al discloses at col. 72, Example 4, a method of contacting a phage F(ab) libraries with a solid support coated human IgE. The phage libraries were constructed by fusing to the

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C-terminal domain of bacteriophage M13g3p by known techniques. The presence of an amber codon between the heavy-chain antibody domain and the g3p domain on phage permits the expression of the phage-displayed fusion protein only in amber suppressor strains of *E. coli*, while soluble F(ab) protein can be obtained with this same construct in non-suppressor strains of *E. coli*. For affinity-selections of phage particles displaying F(ab) variants, phage was prepared by sodium chloride/polyethylene glycol precipitation from *E. coli* culture supernatants. 96-well plastic plates were coated with IgE (human IgE). The IgE solution was then removed, and the plates were incubated with a blocking solution of horse serum. At col. 75, line 45 up to 76, line 43 an assay with an antigen i.e., IgE binding of the phage is discussed. Lowman discloses at col. 58, Example 1 up to col. 60, line 17 a method comprising coating test plates with rat anti-mouse IgG in sodium carbonate buffer, then blocked with bovine serum albumin in phosphate buffered saline. Accordingly, the method steps of Lowman render prima facie obvious the instant claimed method.

Response to Arguments

Applicants submit a 131 declaration describing an experiment encompassing all the steps of claim 1 prior to the effective filing date of Lowman. Applicants submit that the

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reference cannot properly be used as prior art to the present application.

In reply, the 131 declaration of record is insufficient to overcome the reference. The declaration describes specific components used in the method and not the broad components as presently used in the claimed method. Ex parte Biesecker is inapplicable here. It relates to a nonchemical case where a generic claim is sustainable by disclosure of a single species of the genus. The instant case is a chemical and a biotechnological case. Ex parte Jupa, 134 USPQ 573, is controlling. The disclosure of one proportioning of a chemical composition was not considered as supporting generic claims to other proportions.) (" [A] patentee of a **biotechnological** invention cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically enumerated. "). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species....." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004). See also University of California v. Eli Lilly, 43 USPQ 2d 1398, 1405 (1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993).

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University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

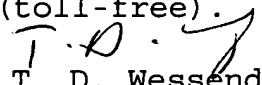
In view of applicants' arguments, the rejection of the claims over Yelton and Huse has been withdrawn in view of the new rejections above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
April 28, 2006